APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 494,282	01/18/2000	Sergey A. Selifonov	02-028930US	3228

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EXAMINER
ZHOU, SHUBO

ART UNIT	PAPER NUMBER
1631	3 7

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)
	09/494,282	SELIFONOV ET AL.
	Examiner	Art Unit
	Shubo "Joe" Zhou	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed
  after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any
  earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is **FINAL**.   2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is
closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *89-104* is/are pending in the application.

  4a) Of the above claim(s) *89-98 and 102-104* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *99-101* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

  If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

  a) ☐ All b) ☐ Some * c) ☐ None of:

  1. ☐ Certified copies of the priority documents have been received.

  2. ☐ Certified copies of the priority documents have been received in Application No. _____ .

  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage
application from the International Bureau (PCT Rule 17.2(a)).

  * See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

  a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)   4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) *6.*   5) ☐ Notice of Informal Patent Application (PTO-152)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *23, 24, 3, 34*   6) ☐ Other: .
  36.

DETAILED ACTION

Applicants' election, with traverse, of Group II (claims 99-101) in the CPA, drawn to a method of identifying a set of oligonucleotides for use in an *in vitro* recombination procedure, in Paper No. 35, filed 10/25/02, is acknowledged. The traversal is on the ground(s) that Group II and III should be examined together because there would be no undue search burden to the Office. This is not found persuasive because, as set forth in the previous Office action, the inventions of Group II and Group III are distinct and classified in distinct classes and have distinct usages. The methods of identifying nucleic acids and a computer system have certainly acquired a separate status in the art as a separate subject for inventive effect and are usually published separately. The search for each of the above inventions is not co-extensive. See page 3. To include Group III for consideration, clearly more classes/subclasses would have to be searched and different search strategies would have to be used, which would cause undue search burden to the office. Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 89-104 are currently pending, but only claims 99-101 are under consideration in the present action, and claims 89-98, and 102-104 are withdrawn from further consideration as being drawn to non-elected inventions.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 139-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Venkatasubramanian et al. (IDS document: J. Chem. Inf. Comput. Sci. Vol. 35, pages 188-195, 1995) in view of Dahiyat et al. (IDS document: US Patent No. 6,403,312).

Claims 99-101 are drawn to a computational method of identifying a set of oligonucleotides for use in an in vitro recombination procedure.

Venkatasubramanian et al. discloses a computational method of designing new chemical polymers using genetic algorithm. The method comprises providing two mating parents of chemical polymer and manipulating the mating parents using such genetic operators as crossover and mutation to produce derivative chemical polymers with desired properties. See page 188, right column, bottom paragraph and page 189, left column. The genetic operators also comprise insertion and deletion. See page 190, left column.

While Venkatasubramanian et al. does not explicitly indicate designing proteins or nucleic acids using the genetic operators, it would have been obvious that an ordinary skill in the art would have been motivated to modify Venkatasubramanian et al. for other polymers such as proteins and nucleic acids because the latter are two major types of chemical polymers and have been studied for centuries by recombination and other mutational methods. There would have been a plethora of prior art references teaching of making novel proteins or nucleic acids by recombination or mutation. For example, Dahiyat et al. disclose a method of protein design

automatic for protein libraries. As an example, Dahiyat et al. teach of a procedure for making

and computationally screening an array of mutant polypeptides of β-lactamase TEM-1. See

columns 30-34. The procedure comprises providing data for the sequence of TEM-1 and

computationally identifying positions of the sequence that are to be allowed to change their

identities (column 30).   The procedure also comprises computationally prescreening on TEM-1

by using Dead End Elimination optimization method to find the lowest energy, ground state

sequences (column 31). The multiple peptide sequences are generated by taking consideration of

the stability of the conformation of the polypeptide and the stability of the conformation of the

enzyme's active site. Also see column 7. To synthesize the recombinant peptide sequences, a set

of overlapping oligonucleotides including all desired mutations are identified and synthesized to

be used to generate a mutant sequence library. See column 32. The method also comprises

additional genetic operations such as PCR multiplication using the identified oligonucleotides,

which would introduce mutations at the various positions selected.

While neither Venkatasubramanian et al. nor Dahiyat explicitly teaches of identifying

frameshift mutations and removing the mutant derivatives as required in the claims,

Venkatasubramanian et al. does indeed disclose ways to let highly fit individuals reproduce more

and "the least fit individuals would be less likely to get selected for reproduction and thus die

eventually". See page 189, left column. Since Venkatasubramanian et al. teaches of using

insertion or deletion as genetic operators, it would have been obvious to an ordinary skill in the

art that such operators would inevitably produce frameshift mutations, some of which would be

less fit and would die out, thus being removed, eventually in the computational procedure.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou, Ph.D.

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